

Evaluation of the Hematologic Profile of Patients Undergoing Chemotherapy who Make use of Hematopoietic Rescue Workers

Fernanda Schwengber¹, Matias Nunes Frizzo²

¹Fernanda Schwengber, Regional University of the Northwest of the State of Rio Grande do Sul.

²Matias Nunes Frizzo, Regional University of the Northwest of the State of Rio Grande do Sul;
matias.frizzo@gmail.com

ABSTRACT

Cytotoxic chemotherapy is directly linked hematologic changes during your anticancer treatment. The hematopoietic rescue agents can be used as supportive care for patients with anemia or neutropenia induced by cytotoxic chemotherapy. This study aimed to evaluate the blood count of patients undergoing chemotherapy and who made use of hematopoietic rescue workers, evaluating hematological changes induced by cytotoxic chemotherapy. This was a retrospective, descriptive and analytical study of the medical records of 36 patients undergoing chemotherapy and who used hematopoietic rescue workers at some time in their anticancer treatment in a High Complexity in Oncology Center. Of the patients included in the study population, 61% are female, and the average age of these is 57,25 years (SD ± 10,84), the most prevalent cancer among patients was the breast (48%), hematological used rescue agent is Filgrastim (53%), Erythropoietin (33%) and Erythropoietin and Filgrastim (14%). The pharmacological class used in anticancer therapy in prevalence is the antimetabolic taxoids and associations, representing 53% of the study population. The results of this study, as well as data from the scientific literature, demonstrate the importance of the use of hematopoietic rescue agents in chemotherapy protocols, due to the proliferative effect / therapeutic these growth factors, which reduce side effects of chemotherapy cytotoxic, giving cancer patients a better quality of life to follow your anticancer treatment, and thus increase the chance of cure.

Keywords: Chemotherapy. Stimulating Factor Granulocyte Colony (G-CSF). Leukopenia. Erythropoietin. Anemia.

CITATION OF THIS ARTICLE

Fernanda Schwengber, Matias Nunes Frizzo. Evaluation of the Hematologic Profile of Patients Undergoing Chemotherapy who Make use of Hematopoietic Rescue Workers .World J. Clin. Pharmacol. Microbiol.Toxicol. Vol 1 [4] November 2015: 30-37

INTRODUCTION

The cancer is known as a disease whose uncontrolled growth of cells invade tissues and organs that share quickly. These tend to be aggressive and uncontrollable determining the formation of malignant tumors with the potential to develop metastasis in different organs of the body (Sarkar et al., 2013).

Nowadays, the cancer has been a serious public health problem in developed and developing countries, deserving increasingly research with finality to get better quality and humanization of care for patients with this disease (Brasil, 2009; Brasil, 2014).

Among the treatment modalities for cancer, the chemotherapy introduces a highest index cure for many tumors, including the most advanced and is one that more increases the survival of cancer patients (Liu; Lin; Yang, 2015). The antineoplastic treatment should be administered preferably in polychemotherapy, for the purpose of to act at different stages of cell division, destroying the cells which have a dysfunction in your the growth process or division. Due to its specificity for the cells that are target, the antineoplastic drugs can reach normal cells that have similar characteristics to the tumor, inducing to depression of bone marrow in different degrees, depending of agent and dose used, causing some secondary effects. Some of these effects are well controlled with appropriate dosages and judicious using from other drug (Henriques, 2010; Ávila; Soares; Silva, 2013; Bonassa,2005).

The polychemotherapy is, normally, able to slowing tumor growth mechanism, to make possible better answers to treatment. Its main advantages are: the additive effect which is produced; the potentiation of the therapeutic effect of a drug with the use of another; retardation of tumor resistance and possibilities of

smaller doses, however, do not prevent the cytotoxic effects that these drugs induce to the body (Pozer et al., 2012; Fernando and Jones, 2015).

The hematologic toxicity is the most important reaction of chemotherapy due to the fact that the hematopoietic tissue shows a high rate of cell proliferation and, your instant consequence is the bone marrow's inability to replace the cellular elements of the circulating blood. This reaction should be monitored during the treatment, because decreases the patients quality of life, getting worse your clinical condition, making it more susceptible to infections and other diseases associated to bone marrow depression. It is of great importance identify and monitor these changes in the patients' blood counts, enabling early diagnosis of leucopenia, thrombocytopenia and anemia, due to the cytotoxic action of these drugs (Brasil, 2008; Bonassa and Gato, 2012; Longo, 2015).

On the other hand to the hematological toxic effects of chemotherapy, the hematopoietic rescue workers are extremely useful in the high dose treatment chemotherapy, they speed and improve the regeneration of normal tissues after the chemotherapy. The rescue workers more used in the medical practice are the hematopoietic growth factors such as, granulocyte stimulator factor (G-CSF), granulocyte / monocyte-macrophages (GM-CSF), by erythrocyte red series (EPO) and platelets growth factor (TPO) (Souza et al., 2000; Bonassa and Gato, 2012; Longo, 2015).

The growth factors which are used as hematopoietics rescue workers are from family of cytokines. The EPO is the principal growth factor that acts about the erythroid line and, regulates the production of red blood cells stimulating their proliferation and differentiation, leading to increased erythrocyte mass, being this growth factor used as an hematopoietic rescue agent in treatment of anemia caused by chemotherapy, reducing the need for transfusion. The high of hemoglobin (Hb) rate and the reducing the necessity for transfusion take to improving the quality of life of these patients (Longo, 2015).

The WBC to start from growth factors G-CSF e GM-CFS. The use of these growth factors has been one of the therapies indicated for treatment of leucopenia of cancer patients, mainly in neutropenia cases in which to practice a great importance in the immune defense of the patient, leaving them less susceptible to infections and improving their clinical condition. These hematopoietics rescue workers are used clinically successfully in cancer patients, which treatment requires high doses of chemotherapy (Braunwald et al., 2002; Kuniechinck, 2013).

The hematopoietics rescue workers should be included in the chemotherapy protocol when the drug used in the câncer treatment will be high grade of cytotoxicity, making the use growth factors as hematopoietics rescue workers of great importance in preventing and treating pancytopenia caused by chemotherapy, allowing that will be held the chemotherapy scheme and enable bigger chance of cancer cure, recovering normal cells affected by treatment (Göller; Wazlawick; Rucker, 2011).

Against of this, that research looked for to evaluate the blood count of patients submitted to chemotherapy who made used of hematopoietics rescue workers. Was evaluated the action of these agents for assisting in the recovery of bone marrow function, causing stimulation in the growth of blood cells that suffered action of chemotherapeutic drugs.

MATERIALS AND METHODS

It is about retrospective study, descriptive and analytical realized with medical records review of patients submitted chemotherapy who used hematopoietics rescue worker at some time in their antineoplastic treatment on a Highly Complex Oncology Center (CACON), that is reference in the care of cancer patients in the Northwest Region of the Rio Grande do Sul State, Brazil. They were chosen 36 patients and from whose medical records were collected the information's for the study. With help of a form were filled the data taken from each history in the period of a year that began in July 2014.

After the data collect, the results of blood counts were associated with chemotherapeutic agents and hematopoietic rescue workers to review the results of descriptive and mathematical-statistical form using absolute frequency and percentage. The review involves the hematologic effects associated with the rescue workers used by patients from CACON, being them the Filgrastim (G-CSF) and the Erythropoietin (EPO), about the hematologic cells counting respective of each agent, being them the WBC and the RBC. For purposes this study we chose to use the values reported by the World Health Organization, that defines anemia as a dosage Hemoglobin (Hb) below 12 g/dL for women and 13 g/dL for men; normal counting of Red Blood Cells (RBC) of 4 to 5,3 $\times 10^6/\text{mm}^3$ for women and 4,5 to 6 $\times 10^6/\text{mm}^3$ for men; White Blood Cells (WBC) totals for the both 4000 to 10000/ mm^3 ; sticks 100 to 500/ mm^3 and segments 2500 to 6500/ mm^3 (WHO, 2001).

Ensuring the ethical principles these study, were not mentioned patient names or other informations that may harm the secret about their identify, as well as to fulfill the Resolution n° 466/2012 the National Health

Council (Brasil, 2012). To sample components were assigned identification numbers, being which collected data were treated statistically. This study was approved by ethics committee for research to Regional University in the Northwest of the Rio Grande do Sul (UNIJUI) through by nº 1.029.415 on April 24, 2015.

RESULTS

For the study were selected 36 patients who made use some hematologic rescue agent as a result from chemotherapy cytotoxic therapy during the 2014 year, in a CACON, by to grow the levels of Hb, RBC and WBC. Just are included in research the patients who had in their medical records the informations about hemogram realized in the pre-chemotherapy period, post-chemotherapy and post-hematopoietics rescue agents.

Of patients included in the study population, 61% were female and 39% were male, with mean age 57,25 (DP \pm 10,84) years, showing minimum age 25 years-old and maxim 83 years-old. In the analysis about the ages of both genders was observed predominance of the ages between 46 and 60 years-old, according to shown the Table 1.

About the analysis on the pathology undergoing chemotherapy met 48% breast cancer, 17% genital system cancer and 14% digestive system cancer. In relation to the pharmacological classes used in antineoplastic therapy found a prevalence of antimetabolites and associations, representing 53% of the study population. The antimetabolite chemotherapy associations are shown in Table 1.

When analyzing the results from the use of hematological rescue workers found the following results: 53% of patients evaluated needed to use Filgrastim, 33% of patients needed to realize the use of EPO and 14% used the both agents for to get hematological regeneration.

Of the 36 patients, just two not realized chemotherapy, only to do use of hematological rescue workers, due to your specific treatment for myelodysplasia, being, excluded from the study. Moreover, 19 patients showing incomplete hematological data, preventing a complete analysis about the previous and later chemotherapy results, and so, after the application of hematological rescue workers. In this way, the final population included in study were 15 patients who showing all the haematological data neede to evaluate the changes about the chemotherapeutic as well as Filgrastim and EPO. The dates of 15 patients were compiled in Table 2, separating the haematologicals data at the moment 1 (pre-chemotherapy period), moment 2 (post-chemotherapy period) and moment 3 (post-application period of Filgrastim and/or EPO). It should be noted that in the moment 2 were applied the agents for then at the moment 3 evaluate the hematological results.

In Table 2 it describes the counting of RBC and Hb levels for patients 1, 2 and 3 who used EPO with hematological rescue agent after cytotoxic action of chemotherapy at the three times of study. For a better view of the variation in RBC counting and Hb levels has done the Picture 2. In the Pictures 3 and 4 were showing the dates about of WBC totals counting and neutrophils in the forms of bat + segmented patients 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15 who made use Filgrastim with hematologic rescue agent.

DISCUSSION

This study evaluated a sample of 36 patients, which was observed the prevalence of female sex, representing 61% of the population of the research, as in the study made by Herr et al. (2013), in which the authors also demonstrate the prevalence of the female gender in the populations. The authors also claim that the prevalence of the female sex in studies about the cancer are characteristics in the literature, corroborating with estimates for the year 2013 indicated an increasing number of new cancer cases in women exceeds the number of new cases in the male population.

The prevalence of breast cancer (48%) and of cancer in the male and female genital organs (17%) also can be demonstrated in the predominance of the female gender in this study. In the study of Göller, Wazlawick e Rucker (2011), the results highlighted the prevalence of the neoplasms located in the male and female genital organs, as well as, also breast tumours. One of the factors associated with prevalence of these tumours is due that fact that in the clinical protocols of treatment of this neoplasm prevail the therapies with antineoplastic of high myelosuppressive potential. The same authors reported similar results the present study on the age group, also demonstrating the prevalence of the range of 46 and 60 years, that represents 50% of the sample of this research, heaving 57,25 as average age (DP \pm 10,84).

In relation to the chemotherapeutic agents most related to the use of some agent of hematopoietic rescue, the pharmacological class that presented higher bone marrow depression was the taxoids antimetabolite and associations that was the antineoplastic therapy of higher prevalence, representing 53% of the population of the study, followed by antimetabolites and associations (14%). The taxoids are introduced in the antineoplastic treatment of several types of cancer. The chemotherapy drugs used in

antineoplastic regimens of this pharmacological class are paclitaxel and analog docetaxel and associations. The antineoplastic activity of this class is based on the cell cycle interruption, stabilizing cellular microtubules, causing apoptosis (Sandra, 2013; Weger; Beijnen; Schellens, 2014).

Most of the patients of this study used taxanes in combination with others chemotherapy drugs, as Doxorubicin and Cyclophosphamide, that in clinical medicine are used as TAC protocol. This combination is performed so that the drug may act at different stages of the cell cycle, promoting greater antitumor activity and with less chance of resistance to chemotherapeutics (Andrade et al., 2013).

The Doxorubicin is an antineoplastic of the family in the cytostatic anthracyclines which has the ability to inhibit the uncontrolled growth of cells, blocking synthesis of DNA. Studies have reported how their toxic effects cardiotoxicity and myelosuppression (Machado et al., 2008). Already the cyclophosphamide is an alkylating antineoplastic agent which is capable to exterminate the tumor cells independent of the cell cycle phase. The haematological toxicity as side effects of these drugs is reported in the study of Ferdinandi and Fereira (Ferdinandi and Ferreira, 2009).

Due to the different characteristics and mechanisms of action of these drugs it is chosen to make use on multidrug chemotherapy, in which different pharmacological classifications of drugs are applied, seeking a broader effect on tumor cells, trying not to raise their level of toxicity (Almeida et al., 2005). Weger, Beijnen e Schellens (2014) in a study of cellular and clinical pharmacology of paclitaxel and docetaxel say that one of the most common toxicities after intravenous administration of these agents is the neutropenia, which is exactly the toxicity most frequently observed in this study, that can be related to the prevalence of this pharmacological class used, leading to the use of hematopoietic rescue agents.

The hematopoietic rescue agents are being used as a clinical routine to regain bone marrow depression caused by cytotoxic chemotherapy. The use of these agents stimulates the development of progenitor cells and allows the continuity of antineoplastic treatment, allowing the maintain uninterrupted treatment protocol, favoring the chances of cure for these patients (Dale, 2002; Held; Hildebrandt; Ludwig, 2010; Schirm et al., 2014).

In the present study the hematopoietic rescue agents used in palliative or prophylactic the recovery of cells affected by cytotoxic chemotherapy were the isolated EPO (33%), the EPO with the Filgrastim (14%) and the isolated Filgrastim (53%). The combined use of these two agents (EPO and Filgrastim) was evaluated in a study by Schirm et al. (2014) the authors reported have found relevant results for the combined use of these agents during chemotherapy.

Two patients in the sample did not use the rescue agents by the cytotoxin induction chemotherapy but rather for presenting myelodysplasia. The hematopoietic growth factor is the class of drugs most widely prescribed for patients with this disease, to improve some of the signs and symptoms of bone marrow failure associated with myelodysplasia (Steensma, 2011).

EPO is an agent used for anemia induced by chemotherapy, stimulating the division and differentiation of erythroid progenitor cells by reducing the need for blood transfusion (Held; Hildebrandt; Ludwig, 2010). Filgrastim is an agent with G-CSF and clinical guidelines recommend the use of this agent in patients at high risk of neutropenia. The neutropenia and its infectious complications represent the dose-limiting toxicity of most common cancer chemotherapy (Dale, 2002).

After detailed analysis of the study patients was obtained only 15 patients contained in its historical all necessary information for statistical analysis of laboratory tests, of which were collected test results in three times of antineoplastic treatment, as well as in the study by Göller, Wazlawick e Rücker (2011), where the authors also seek in the blood count results, which at first was found normal levels of WBC in the exams of these patients before the initiation of cytotoxic chemotherapy; the second time the significant reduction of these cells by antineoplastic drug use; and the third time the restoration of normal levels of the cells after the use of G-CSF rescue agent. In this study, so the results were evaluated referring to the three times so we could make comparisons between bone marrow depression induced by chemotherapy and rescue these cells after use of hematopoietic rescue agents.

The patients 1, 2 and 3 were the ones who made use of EPO as a rescue agent after cytotoxic chemotherapy and only patient 1 did use in isolation. In chemotherapy the anemias can be induced by inflammatory cytokines that suppress erythropoiesis and inhibit the production of EPO. In this context the inhibition of EPO production promotes a reduction in the proliferation of progenitor cells of the red series, because the EPO is the principal hormone regulating erythropoiesis. In the absence of EPO forming unit RBC colony just not developing, being one of the causes of anemia (Robert; Carol; Zoe, 2007).

According Rodgers et al. (2013) to anemia can be prevalent in 30% to 90% of reduced Hb, before starting treatment with cytotoxic chemotherapy, according to Table 2. Afterwards the application of chemotherapy concentrations of Hb of the patients 1 and 2 reduced to 8.6 g / dL and 7.9 g / dL respectively. After using

EPO all patients showed significant improvement in their erythrocyte and Hb levels, as well as other studies demonstrates (Michallet et al., 2014). The use of EPO as hematopoietic rescue agent after cytotoxic chemotherapy improves the Hb levels, lowering levels of anemia, prevents the appearance of clinical complications, improves the quality of life of patients and reduces the need for blood transfusion, which may generate immunological complications.

The patients who used the G-CSF with Filgrastim (Table 1) in its first phase (before chemotherapy) had WBC values within the normal range, which is suitable conditions for application of chemotherapy sessions, except for patient 3 that already presented himself leucopenics. The leucopenia is caused usually by dropping of neutrophils (neutropenia) induced by the underlying disease or the treatment (Zago; Falcão; Pasquini, 2003). In the present study it can be observed leucopenia directly related to neutropenia in Figures 3 and 4, in which initially verified the global count of WBC and subsequently the specific neutrophil count.

The Haematological response caused by Filgrastim consists in neutrophils, namely an increase in the number of circulating neutrophils, from the proliferation and accelerated differentiation of precursor bone marrow cells in differentiated neutrophils (Moraes, 2004). It is observed in white cell counts that growth factor significantly accelerate neutrophil recovery rate following myelosuppressive chemotherapy in intensive doses, reduces the duration of neutropenia and in this way increases the minimum concentration of neutrophils observed after a course of chemotherapy (Ria et al., 2013).

In figures (3 and 4) demonstrated that the total results of WBC and neutrophils (rod + segmented) respectively, observed that in the second time of antineoplastic treatment, in which patients have performed cytotoxic chemotherapy and there is a reduction in WBC levels in the case of this study was a reduction in 100% of patients evaluated. Already the neutropenia was also observed, but did not present itself in all patients. These results corroborate about the myelosuppressive effects of chemotherapeutic agents.

In the international classification that quantifies the hematological toxicity of cancer treatment, NCI-CTCAE, which uses a scale of 1-5, 1 representing low toxicity and 5 the patient's death second scale the normal levels of neutrophils are 3000-7000 cel./mm³, grade 1 of hematological toxicity is 3000-1500 cel./mm³, followed by grade 2 (<1500-1000 cél./ mm³), grade 3 (<1000-500 cél./ mm³), and grade 4 (<500 cél./ mm³) (Robert; Carol; Zoe, 2007).

The patients 3, 6, 9, 14 and 15 presented a decrease in levels of severe neutrophils, getting between grades 3-4 of hematologic toxicity induced by cytotoxic chemotherapy. Clinically these information are very important, because as the smaller the absolute count of neutrophil and higher duration of neutropenia, the greater the susceptibility to an infection occurs. Neutropenic cancer patients with a count lower than 500 cells./mm³ presents a high risk for contracting serious infections including because they are predisposed by other factors such as mucositis, venous access and multiple hospitalizations⁽³⁶⁾.

Another aspect to be highlighted is that the neutropenia predispose the occurrence of febrile neutropenia and this is usually a life threatening complication of chemotherapy, in which fever may be the only symptom. The febrile neutropenia is defined as a temperature measurement above 38,3°C or a temperature maintained above 38°C for one hour in a patient who suffers from severe neutropenia. This type of fever indicates and infection that can put the patient at risk of life and requires immediate intervention of antibiotics, as well as all risks posed. Besides that, immunological complications lead to dose reduction or delay in chemotherapy treatment, which will compromise its effectiveness (Hoggatt et al., 2015).

The patients 7 and 10 presented no neutropenia after cytotoxic action of chemotherapy, these had normal neutrophil values before the antineoplastic therapy. However, the other patients (2, 4, 5, 8, 11, 12, 13), had a decrease in the neutrophil counting, approaching the levels recommended references in this study. When assessing only the third moment, in which we use the hematopoietic recovery agent Filgrastim, obtained the recovery in neutrophil counts, demonstrating a good bone marrow response. The patients 4, 8, 11 and 12 show an increase in total WBC count and neutrophils, but some still remained leucopenics. Already the patients 5 and 13, raise significantly the WBC count, surpassing the limits of references (19000 – 13400 céls./ mm³), proving the scientific data on the high medullary response of hematopoietic recovery agent.

Göller, Wazlawick and Rücker (2011), describing similar results to this study, because before chemotherapy, the patients had normal white blood cell count, of which they became leukopenic after the cytotoxic protocol and established WBC counting after therapy with Filgrastim. Based on the results of this study, however that the sample has been reduced, Filgrastim therapy allows the degree and duration of neutropenia be reduced and that a greater percentage of patients to be able to complete a full protocol of chemotherapy, providing a higher cure rate to cancer.

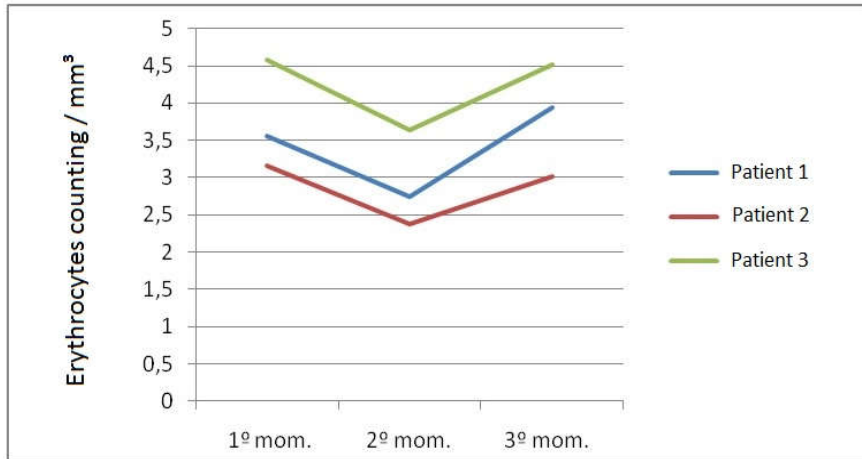
Table 1: Characteristics of patients included in the study

	Total Patients = 36	%
Sex		
Female	22	61
Male	14	39
Age		
≤ 30	1	3
31-45	2	6
46-60	18	50
≥ 60	15	41
Tumor Classification		
Genital organs Male and Female	6	17
Brest	17	48
Digestive system	5	14
Lung	4	11
Myelodysplasia	2	5
Others	2	5
Rescue Agent Used		
EPO	12	33
EPO and Filgrastim	5	14
Filgrastim	19	53
Pharmacological Class of Antineoplastic Agents In the moment Used in Study		
Alkylating agents and associations	3	9
Antimetabolites and Associations	5	14
Antimitotic taxoids isolated	2	5
Antimitotic taxoids and associations	19	53
Others	5	14
Do not chemotherapy	2	5

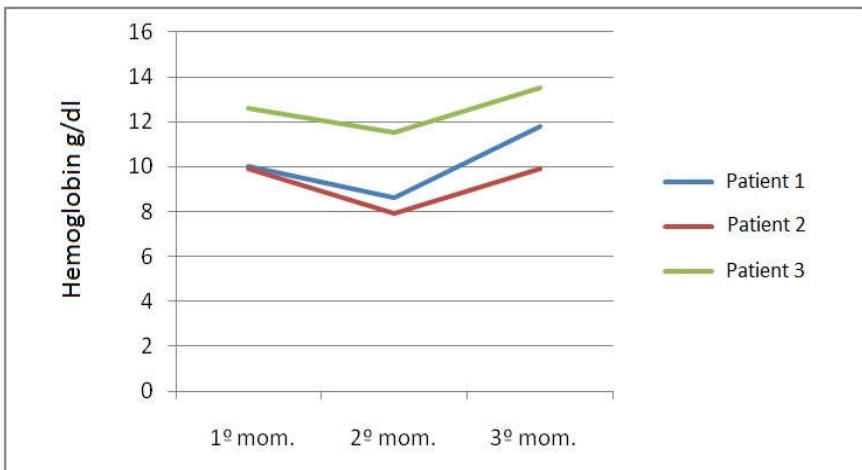
Table 2: Analysis of tests carried out at three different times of antineoplastic treatment, referring to the patients included in the study

Patients / Gender	RBC (/mm ³)			Hb (g/dL)			WBC (/mm ³)			Segmented +Rod Cells (/mm ³)			Rescue Agent
	1° M	2° M	3° M	1° M	2° M	3° M	1° M	2° M	3° M	1° M	2° M	3° M	
1/F	3,56	2,74	3,94	10,0	8,6	11,8	4300	3000	3800	3096	1500	1862	EPO
2/M	3,16	2,38	3,01	9,9	7,9	9,9	3500	1400	7900	1505	1036	6241	Filgrastim and EPO
3/F	4,58	3,64	4,51	12,6	11,5	13,5	2600	1200	6100	1638	228	5363	Filgrastim and EPO
4/F	4,48	4,56	3,82	13,8	13,8	11,8	5700	4200	4100	4218	2562	2788	Filgrastim
5/F	3,56	3,63	4,00	10,0	10,7	11,5	4300	3400	1900	3096	1426	1653	Filgrastim
6/M	4,07	2,93	3,52	10,9	9,4	11,4	7600	1400	3700	5472	436	1831	Filgrastim
7/M	5,30	3,82	3,71	15,6	10,7	10,3	7500	7400	8700	4875	5782	7308	Filgrastim
8/F	4,74	4,34	3,47	13,4	13,2	10,0	5200	3700	7300	2756	2109	5548	Filgrastim
9/F	4,05	3,47	3,46	12,0	11,0	11,4	5500	1800	3100	3844	514	1680	Filgrastim
10/M	4,46	4,72	4,86	12,9	13,9	13,1	6900	4900	7400	5520	3773	5254	Filgrastim
11/F	3,47	3,27	3,28	11,1	10,3	10,0	4300	3100	3700	2279	1767	3212	Filgrastim
12/M	4,79	4,22	4,73	14,4	11,7	13,6	6760	4100	6700	4124	2911	4221	Filgrastim
13/F	3,60	3,29	3,53	9,8	10,3	11,4	3900	3200	1340	2847	1760	10361	Filgrastim
14/F	4,02	3,47	3,46	12,0	11,0	11,4	5440	1700	3000	3942	612	1710	Filgrastim
15/F	4,22	4,02	4,29	11,7	12,0	13,2	4100	1500	2510	2911	450	1330	Filgrastim
Média	4,13	3,63	3,83	12	11,06	11,62	5173	3066	6694	3474	1791	5015	
Desvio Padrão +-	0,59	0,66	0,54	1,78	1,72	1,26	1505	1690	4473	1243	1504	4074	

(* 1 M - pre-chemotherapy, 2nd M - after chemotherapy; 3 M - after hematopoietic recovery agent)

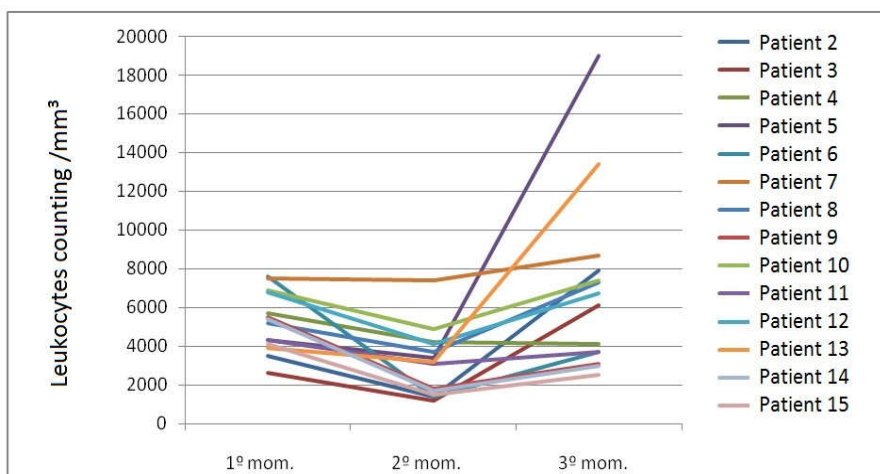


(* 1 mom - pre-chemotherapy; 2nd mom - post-chemotherapy;.. 3rd mom - after hematopoietic recovery agent)
Figure 1: Analysis of RBC values in previous tests to chemotherapy, during and / or after chemotherapy and after the use of EPO



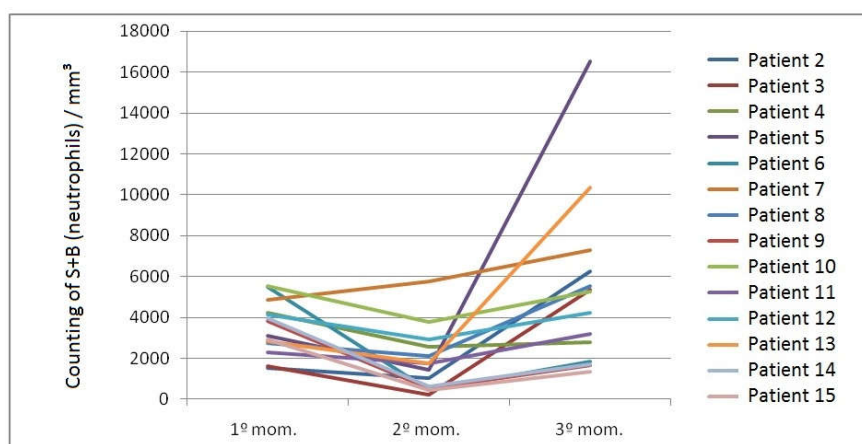
(* 1 mom - pre-chemotherapy; 2nd mom - post-chemotherapy;.. 3rd mom - after hematopoietic recovery agent)

Figure 2: Analysis of Hb levels in previous exams to chemotherapy, during and / or after chemotherapy and after the use of EPO



(* 1 mom - pre-chemotherapy; 2nd mom - post-chemotherapy;.. 3rd mom - after hematopoietic recovery agent)

Figure 3: Analysis of WBC values in previous exams to chemotherapy, during and / or after chemotherapy and after the use of Filgrastim



(* 1º mom - pre-chemotherapy; 2º mom - post-chemotherapy; 3º mom - after hematopoietic recovery agent)
Figure 4: Analysis of neutrophil values (segmented + rod cells) in previous exams of chemotherapy, during and / or after chemotherapy and after the use of Filgrastim

CONCLUSION

The results of this study, as well as the data from the scientific literature, demonstrate the importance of the use of hematopoietic rescue agents in the chemotherapy protocols, due to the proliferative/therapeutic effect of these growth factors, which reduce the side effects of cytotoxic chemotherapy, giving cancer patients a better quality of life to follow your anticancer treatment, and increase the chance of cure.

Must be emphasized that even with the small number of patients evaluated in this study showed to be important clinical data on the toxicity arising from chemotherapy and the importance of the use of hematopoietic rescue agents for the recovery of cancer patients and continuity of anticancer treatment which open questions and perspectives for further studies on the use of these agents in clinical oncology.

REFERENCES

- Sarkar, S., Horn, G., Moulton, K., Oza, A., Byler, S., Kokolus, S., Longacre, M. 2013. Cancer development, progression, and therapy: an epigenetic overview. *Inter J Mol Sci.* 14(10): 21087-21113.
- Brazil. Ministry of Health. National Cancer Institute. Estimate 2010: cancer incidence in Brazil. Rio de Janeiro: INCA; 2009.
- Brazil. Ministry of Health. National Cancer Institute. Estimate 2010: cancer incidence in Brazil. Rio de Janeiro: INCA; 2014.
- Liu, H. Lin, L.V., Yang, K. 2015. Chemotherapy targeting cancer stem cells. *Am J Cancer Res* 5 (3): 21-34.
- Henriques, M.C.L, Rodrigues, S.D., Gonçalves, L.C, Almeida, A., Santos, A.H.S., Abud, A.C., Teixeira, A.S., Barros, A.M.M. 2010. Self-care: the practice of women with breast cancer undergoing chemotherapy. *Rev. Enferm. UERJ.* 18 (4): 638-643.
- Avila, F. F., Soares, M.B.O., Silva, S.R. 2013 Profile hematology and serum biochemistry in patients undergoing cancer chemotherapy. *Rev Enf Aten Health* (2): 32-45.
- Bonassa, E.M.A, Santana, T. R. 2005. Nursing in cancer therapy. (Eds) Atheneu. Sao Paulo; 235-298.
- Pozer, M.Z., Silva, T., Regino, P.A, Junior, P.C.F, Silva, S.R. 2012. Signs and symptoms of myelosuppression chemotherapy at home, among women with gynecologic cancer. *Cienc, Care and Health* 11 (2): 148-198.
- Fernando, J. and Jones, R. 2015. The principles of cancer treatment by chemotherapy. *Surgery (Oxford).* 33 (3): 131-135.
- Brazil. Ministry of Health. National Cancer Institute. Nursing interventions for cancer control: a proposal for teaching-service integration. Rio de Janeiro: INCA; 2008.
- Bonassa, E.M.A. and Cat, M.I.R. 2012. antineoplastic Schemes, oncological therapy to nurses and pharmacists. (Eds) Atheneu. Sao Paulo; 165-189.
- Long, D.L. 2015. Cytokine: Growth factors and immunologic intervention. *Harrison Oncology manual.* (Eds) McGraw-Hill. Porto Alegre; 345-372.
- Souza, C.A., Vigorito, A.C. Spider F.J.P, Oliveira, U.K., Eid, K.I.B., Ruiz, M. 2000. Therapeutic cytoprotective in patients treated with chemotherapy and / or radiotherapy antineoplastic. *Rev. Bras. Hematol. Hemoter.* 22 (2): 123-128.
- Kuniechinck, N. 2013. stimulating factor Production of recombinant human granulocyte colony (RHG-CSF) in bioreactors. Phd Thesis Pontificia Catholic University of Rio Grande do Sul, Porto Alegre, Brazil.
- Braunwald, D.L. Kasper, A.S. Fauci, J. Larry J., Dan L. Longo, S. H. 2002. *Harrison internal medicine.* (Eds) McGraw-Hill. Rio de Janeiro, 321-361

16. Göller, F. F., Wazlawick, M., Rücker, B. 2011. Effects and importance of using stimulating factor granulocyte colony (G-CSF) in cancer patients undergoing cytotoxic chemotherapy. *Infarma Pharmaceutical Sciences*. 23 (7-8): 8-14.
17. World Health Organization. (2001). Iron deficiency anemia. Assessment, prevention and control. A guide for program managers. Geneva.
18. Brazil. National Health Council. Resolution No. 466 of 12 December 2012. [out access in 2014]. Available at: <<http://conselho.saude.gov.br/resolucoes/2012/Reso466.pdf>>.
19. Herr, G. E., Kolankiewicz, A.C.B., Berlezi, M.S., Gomes, J. S., Magnago, T.S.B.D.S., Rosanelli, C.P., Loro, M.W. 2013. Evaluation of knowledge about cancer disease and care practices with health. *Rev. Bras. Cancerol*. 59 (1): 33-41.
20. Sandra, R.N. 2013. Evolution of taxanes in the treatment of metastatic breast cancer. *Cli J Oncol Nur*. 17 (1): 1-9.
21. Weger, V.A., Beijnen, J. H., Schellens, J.H.M. 2014. Cellular and Clinical Pharmacology of the taxanes docetaxel and paclitaxel-a review. *Anti-Cancer Drugs*. 25 (5): 488-494.
22. Andrade, DAP, Zucca-Matthes, G., Vieira, RAC, Andrade, C.TA., Costa, AM, Monteiro, AJC, Dal Lake, L. Nunes, JS 2013. neoadjuvant chemotherapy and pathological response: Cohort retrospective. *Einstein*: 11 (4): 1-9.
23. Machado, V., Cabral, A., Monteiro, P. Gonçalves, p., Providencia, L. 2008. Carvedilol as protector of cardiotoxicity induced by anthracyclines (doxorubicin). *Rev Port Cardiol*. 27 (10): 1277-1296.
24. Ferdinandi, D.M. and Ferreira, A.A. 2009. alkylating agents: hematologic adverse reactions and complications. *AC & T Research*. 1 (1): 1-12.
25. Almeida, VL, Piglet, A., Reina, LLB, Montanari, CA, Donnici, CL, Lopes, MTP 2005. Cancer and specific cell cycle-specific anticancer agents and non-cell cycle that interact with DNA: an introduction . *Quim Nova*. 28 (1): 118-29.
26. Held, T. K., Hildebrandt, M.O., Ludwig, W. D. 2010. Hematopoietic growth factors. Possibilities and limitations. *Der Internist*. 51 (7): 863-71.
27. Dale, D.C. 2002. Colony-stimulating factors for the management of neutropenia in cancer patients. *Drugs*. 62 (1): 1-15.
28. Schirm, S. Engel, C., Loefflerand, M. Scholz, M. 2014. The combined model of human Erythropoiesis and granulopoiesis under growth factor and chemotherapy treatment. *Mod Theor Biol Med* 11 (1):. 1-24.
29. Steensma, S.E. 2011 Hematopoietic Growth Factors in myelodysplastic syndromes. *No in Oncol*. 38 (5): 36-50.
30. Robert I., Carol V., Zoe, N. 2007. Mosby's oncology drug reference. Mosby. (Eds) Elsevier. 2: 126-156.
31. Rodgers, GM, Becker, PS, Blinder M, Cella, D., Chanan-Khan, A., Cleeland, C., Coccia, PF, Djulbegovic, B., Gilreath, JA, Kraut, EH, Matulonis , AU, Millenson, MM, Reinke, D., Rosenthal, J., Schwartz, RN, Soff, G. Stein, RS, Vlahovic, G. Weir, AB 2013. Cancer and chemotherapy induced anemia. *NCCN Clinical Practice Guidelines in Oncology*. 10 (5): 628-653.
32. Michallet, M., Luporsi, M., Soubeyran, P., Ali Amar, P. Boulanger, V., Carreiro, M., Dourthe, L., Labourey, J., Lepille, D., Maloisel, D., Mouysset, J., Nahon, S., Narcissus, B., Nouyrigat, P., Sakek, N., Albrand, H. 2014. biosimilars in the management of anemia secondary to chemotherapy in hematology and oncology: results of the ORHEO observational study. *BMC Cancer* 14 (1): 503-512.
33. Zago, M.A., Falcão, R. P., Pasquini, R. 2003. Hematology: fundamentals and practice. (Eds) Atheneu: São Paulo, 771-796.
34. Moraes, A.A.G. 2004. Growth factors in clinical oncology. *Bras J Clin Oncol*. 1 (3): 43-49. Ria, R., Reale, A., Moschetta, M., Dammacco, F., Vacca, A. 2013. Neutropenia and G-CSF in lymphoproliferative diseases. *Hematology*.18(3):131-137.
35. Hoggatt, J., Tiffany, A. Tate, M., Louis, M. 2015. Role of lipegfilgrastim in the management of chemotherapy-induced neutropenia. *Inter J nanomed*.1(10): 26-47.

CONFLICT OF INTEREST	: Nil
Received	: 12.05.2015
Accepted	: 19.10. 2015



The entire article published by World Journal of Clinical Pharmacology, Microbiology and Toxicology is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License Based on a work at www.wjcpmt.com